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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/601,561	12/15/2000	Thomas D. Schneider	15280-3321PC	5945

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EXAMINER

ZHOU, SHUBO

ART UNIT PAPER NUMBER

1631

DATE MAILED: 02/13/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/601,561

Applicant(s)

SCHNEIDER ET AL.

Examiner

Shubo "Joe" Zhou

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 26 November 2001.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-65 is/are pending in the application.
- 4a) Of the above claim(s) 12,15-33,43,64 and 65 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-11,13,14,34-42 and 44-63 is/are rejected.
- 7) ☒ Claim(s) 34 and 40 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 15 December 2000 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 8.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

### **DETAILED ACTION**

Applicant's amendment and request for reconsideration in Paper #9, filed on 11/26/02, and Paper #10, a declaration by Thomas Schneider and Paul Hengen under 37 C.F.R. 1.132, filed on 1/30/02, are acknowledged and the amendments entered.

Applicant's arguments in response to the previous Office Action, mailed 6/19/01, and the declaration have been fully considered. In light of the declaration under 37 C.F.R. 1.132, which declares that Thomas Schneider and Paul Hengen are the sole inventors of the subject matter of Hengen et al. (Nucleic Acids Research, 1997, Vol. 25, pages 4997-5002), the rejection of claims 1-11, 13-14, 34-42 and 44-63 under 35 U.S.C. 103(a) in the previous Office action is withdrawn. The following rejections and/or objections are either reiterated from the previous Office action, or newly applied, and constitute the complete set presently being applied to the instant application. Other rejections and/or objections from the previous Office action not reiterated herein are hereby withdrawn.

Claims 1-65 are currently pending and claims 1-11, 13-14, 34-42, and 44-63 are under consideration.

### ***Claim Rejections-35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

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**Claims 1-3, 6, 8-9, 11, 34-36, 38-40, 42, 51-54, 57-59, and 61 are rejected under 35 U.S.C. § 102(b) as being anticipated by Gille et al. (IDS document: Nucleic Acids Research, Vol. 19, pages 4167-4172, 1991).**

Claims 1-3, 6, 8-9, 11, 34-36, 38-40, 42, 51-54, 57-59, and 61 are drawn to system/compositions comprising nucleic acids and proteins capable of binding thereto, or to methods of performing such binding.

Gille et al. discloses a system/composition and method for performing DNA/protein binding. The system/composition comprises DNA and proteins including FIS and DnaA, wherein the DNA comprises a FIS binding site and an adjacent DnaA binding site (R3), and the proteins bind to their corresponding sites in a mutually exclusive manner. See page 4167, Abstract, and page 4170, right column. Gille et al. also discloses that the DNA used for the binding assay between the proteins and the DNA is "restriction fragments". See page 4168. It is well known to, and readily recognized, by an ordinary skill in the art that "restriction fragments" are double stranded DNA unless made single stranded by a denaturation procedure upon restriction. However, Gille et al. does not disclose such a denaturation procedure. Therefore, Gille et al. implicitly discloses that the DNA is double stranded.

Gille et al. also discloses that "the consensus sequences for FIS and the DnaA box R3 are immediately adjacent to each other", and DNase I protection shows that the two sites overlap by 8-10 bp. See page 4169, right column. This reads on the limitations that the first binding site is within 20 nucleotides, or 11 nucleotides of the second binding site, as required in the instant claims.

While Gille et al. does not explicitly disclose that the difference between the FIS binding site and the DnaA binding site is more than zero bits as required in the instant claims, such is an inherent property of the binding sites. "A bit", as defined by Herman and Schneider (IDS document: Journal of Bacteriology, Vol. 174, pages 3558-3560, 1992), "is the amount of

information needed to choose one of two possible outcomes.” For a binding between protein and DNA, “if a base is always a T, then two bits are required to store that information in a computer. If a base can be anything, then zero bits are required. Therefore, the information content reflects the biological conservation in a binding site.” See page 3558, the paragraph bridging the left and right columns. Given the fact that FIS and DnaA bind to their respective sites in a mutually exclusive manner, and the sequences obtained by DNase I protection, as disclosed by Gille et al., it is clear that the two sites are different and thus have different bits of information. Thus, inherently, the difference between the two is more than zero.

***Claim Rejections-35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

**Claims 1-11, 13-14, 34-42, and 44-63 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gille et al. (IDS document: Nucleic Acids Research, Vol. 19, pages 4167-4172, 1991) in view of Schneider (IDS document : J. Theor. Biol., vol. 148, pages 125-137, 1991) and Schneider (IDS document : Nanotechnology, Vol.5, pages 1-18, 1994).**

For claims 1-3, 6, 8-9, 11, 34-36, 38-40, 42, 51-54, 57-59, and 61, see the rejection under 35 U.S.C. 102 set forth above.

As to claims 4-5, 7, 10, 13-14, 37, 41, 44-45, 55-56, and 60, Gille et al. does not explicitly disclose that the first site and the second site have the same sequences, or contain the sequence of SEQ ID NO:1 or 2 or 3, nor does Gille et al. explicitly disclose binding protein of EF-tu. It is well known in the art that different molecular system can be used for the logical

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operations and computation by molecular machines. For instance, Schneider (1991) discloses that the lac repressor protein and the operator it binds to can be used for such a purpose because lac repressor only binds to its operator when it does not bind to an inducer. EF-tu is another protein that is well known in the art to bind to its DNA sequences. Further, Schneider (1994) teaches molecular computation systems, and states that "genetic control systems often work by one molecule binding to a spot to prevent another molecule from binding there". Schneider further teaches ways of building a molecular computer including using natural genetic control systems and designing new systems based on knowledge of genetic system and selection. See page 15, left column. An ordinary skill in the art would have been motivated by Schneider to modify Gille et al. to test different genetic systems including EF-tu. As to the instant SEQ ID NOs:1-3, as set forth in the previous Office action, the essential parts of sequences of the instant SEQ ID NOs: 1-3 are Fis binding sites as disclosed by Gille et al. with different spacing between the Fis sites, 11 base pairs in the case of SEQ ID NO:2 and 7 in SEQ ID NO:3. Such artificial nucleic acids, which contain the same essential binding site by Fis as disclosed by Gille et al., would have been obvious to one of ordinary skill in the art because adding a linker would not change the binding of Fis. Further, selection of a proper length of linker so as to permit binding of one Fis and prevent the binding of another Fis would have been obvious as Schneider motivates finding a system where binding of one molecule prevents the binding of another.

**Claims 46-50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gille et al. (IDS document: Nucleic Acids Research, Vol. 19, pages 4167-4172, 1991) in view of Wickens et al. (US patent no. 5,677,131, date of patent: Oct. 14, 1997, date of filing: Jul. 9, 1996).**

Claims 46-50 are drawn to a system with the DNA binding protein fused to a trans-activator Gal4.

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Gille et al. does not explicitly disclose such fusion protein. However, fusing a trans-activator such as Gal4 has long been well known the art for studies of protein/protein or nucleic acid/protein interactions. For instance, Wickens et al. discloses a system for studies of RNA/protein interaction, where the RNA binding protein is fused to transactivator Gal4, which activates a reporter gene. The reporter system is a convenient system for monitoring the RNA/protein interaction. See Abstract, Figs. 1A-1C, and columns 5-8. An ordinary skill in the art would have been motivated by Wickens et al. to modify Gille et al. to fuse the Fis protein to Gal4 and a reporting system to take advantage of an easy convenient assay for monitoring the binding between proteins and their binding sites.

#### ***Claim Objections***

Line 12 of claim 34 contains a period "." between the word "said" and "first". This is objected to because each claim is allowed to have only one period, which is at the end of the claim.

#### ***Claim Objections, Warning***

Applicant is advised that should claim 39 be found allowable, claim 40 will be objected to under 37 CFR 1.75 as being a duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

#### ***Conclusion***

No claim is allowed.


Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703) 308-4242 or (703)305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to:  
Shubo "Joe" Zhou, Ph.D., whose telephone number is (703) 605-1158. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on (703) 308-4028.

Any inquiry of a general nature or relating to the status of this application should be directed to Patent Analyst Tina Plunkett whose telephone number is (703)-305-3524, or to the Technical Center receptionist whose telephone number is (703) 308-0196.

S. "Joe" Zhou, Ph.D.



Patent Examiner



MICHAEL P. WOODWARD  
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